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Dkt. No.: 8325-1004
M4-US1

PATENT

CERTIFICATE OF MAILING PURSUANT TO 37 CFR § 1.8

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11/9/05
Date

Michelle Hobson
Signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

WANG et al.

Serial No.: 09/636,243

Filing Date: August 10, 2000

Title: DIMERIZING PEPTIDES

Examiner: T. Wessendorf

Group Art Unit: 1639

Confirmation No: 6438

Customer No.: 20855

TRANSMITTAL LETTER

Mail Stop Appeal Brief
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313

Sir:

Transmitted herewith for filing, please find the following documents:

- X Reply Brief (13 pages) with attached Claims Appendix (2 pages)
- X Return receipt postcard.


The fee is calculated as follows:

	NO. OF CLAIMS	CLAIMS PREVIOUSLY PAID FOR	EXTRA CLAIMS	RATE	FEE
Total Claims	3	- 20	0	x \$50.00	\$0
Independent Claims	1	- 4	0	x \$200.00	\$0
Multiple dependent claims not previously presented, add \$290.00					\$0
Total Amendment Fee					\$0
Petition for Extension of Time Fee					\$0
Small Entity Reduction (if applicable)					\$0
TOTAL FEE DUE					\$0

The Commissioner is hereby authorized to charge any appropriate fees under 37 C.F.R. §§1.16, 1.17, and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 18-1648.

Respectfully submitted,

Date: November 9, 2005

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REPLY BRIEF

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REPLY BRIEF

Mail Stop Appeal Brief
Commissioner for Patents
Alexandria, VA 22313

Sir:

Pursuant to Section 41.37(c) (69 Fed. Reg. 49962, Aug 2004), Applicants submit the following Reply Brief in Response to the Examiner's Answer mailed on September 9, 2005.

This Reply Brief is submitted within two months of the date of mailing of the Examiner's Answer, namely by November 9, 2005. Appellants respectfully request that the decision of the Examiner be reversed.

STATUS OF THE CLAIMS

Claims 5, 6 and 20 are currently pending in the above-referenced case (hereinafter "the application"). The application was originally filed on August 10, 2000 with claims 1 to 19. A substitute specification and preliminary amendment were filed on January 30, 2001. The Office approved the substitute specification and, subsequent to approval, a Restriction Requirement was mailed on July 25, 2002. In a Response to Restriction Requirement, dated August 26, 2002, claims 5 and 6 were elected with traverse. In an amendment filed on December 19, 2002, claims 5 and 6 were amended and claim 20 was added. No amendments to the claims have been entered since, accordingly, claims 5, 6 and 20 are pending as shown in the Claims Appendix. All pending claims remain rejected under 35 U.S.C. § 112, first and second paragraphs and under 35 U.S.C. § 102.

GROUND OF REJECTION

1. Claims 5, 6 and 20 stand rejected under 35 U.S.C. § 112, 1st paragraph as not being adequately described by the specification as filed.
2. Claims 5, 6 and 20 stand rejected under 35 U.S.C. § 112, 2nd paragraph as indefinite.
3. Claims 5 and 20 stand rejected under 35 U.S.C. § 102(b) as anticipated by Pomerantz et al. (1998) *Biochemistry* 37(4):965-970 (hereinafter "Pomerantz").

Appellants note that the Examiner's Answer indicated that two issues (whether drawings were added to the substitute specification and whether the substitute specification was unduly confusing) addressed in the original and Supplemental Appeal Briefs were not appealable. Appellants will Petition these matters as required by the Examiner.

ARGUMENTS

1. The Appeal Brief Contains a Correct Statement of the Status of the Amendments

In the Examiner's Answer it was asserted that the status of the amendments contained in the Appeal brief was incorrect because the amendments after final filed on May 12, 2003 had not been entered. (Examiner's Answer, page 2, paragraph 4).

In fact, the Appeal Brief (filed August 5, 2003, at pages 2-3) clearly noted that the amendments made in a response filed May, 2003 had **not** been entered. In addition, the Claims Appendix of the original Appeal Brief clearly showed that Appellants were aware that the amendments made after final were not entered. Thus, the statement in the Appeal Brief regarding the Status of the Amendments was correct as filed.¹

2. The Claimed Subject Matter

Before addressing the statements in the Examiner's Answer, Appellants wish to clarify the Examiner's apparent misunderstanding of the claimed subject matter. It appears, from parenthetical comments on pages 8 and 10 of the Examiner's Answer, that the Examiner believes that the claims are directed to complexes in which zinc finger proteins are covalently linked by a peptide. This is not the case. The presently-pending claims clearly recite a complex comprising two or more fusion proteins (See Claims Appendix, claim 5). Covalent linkage of two proteins would, of course, result in the production of a single protein, distinct from the claimed multiprotein complexes.² Thus, the claims are directed to complexes comprising two or more proteins that are non-covalently joined via specific binding of non-naturally occurring dimerizing peptides.

¹ Appellants note that the text of claim 6, as presented in the Appeal Brief of August 5, 2003 and the Supplemental Appeal Brief of January 20, 2004, was incorrect. The correct text of claim 6 is presented in the Claims Appendix attached to this Reply.

² Indeed, the originally-presented claims recited a complex comprising a first fusion protein and a second fusion protein, which language was rejected by the Examiner as allegedly indefinite (Office Action of September 25, 2002 at page 8).

3. The Specification Describes the Claimed Subject Matter

Appellants incorporate herein all arguments set forth in the original Appeal Brief (filed August 5, 2003) and the Supplemental Appeal Brief (filed January 20, 2004). Rather than reiterate each argument herein, Appellants address various assertions set forth in the Examiner's Answer, mailed more than a year and half after the Supplemental Appeal Brief was filed.

The Examiner Answer's again maintained that the specification as filed did not adequately describe claims 5, 6 and 20. In particular, the Examiner alleges that the specification does not adequately describe:

- (1) zinc finger proteins and
- (2) non-naturally-occurring dimerizing peptides.

In response, Appellants submit that the assertions that the zinc finger proteins and the non-naturally-occurring dimerizing peptides of the non-covalently linked complexes are not adequately described are legally and factually unsustainable. Legally, the assertions ignore the critical axioms of a written description inquiry, namely that the written description is presumed to be satisfied at the time of filing and, moreover, that the original claims (along with literal description in the specification in the form of text or drawings) are irrefutable evidence that the specification adequately described the claimed subject matter. *See, e.g., In re Wertheim*, 191 USPQ 90, 98 (CCPA 1976); *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991). The Patent Office's own Training Materials on Written Description emphasize that when a single species or embodiment is disclosed in support of originally claimed subject matter, the written description requirement can be met. *See*, Written Description: Original Claims: Decision Tree, Synopsis of Application of Written Description Guidelines, pages 7 and 8.

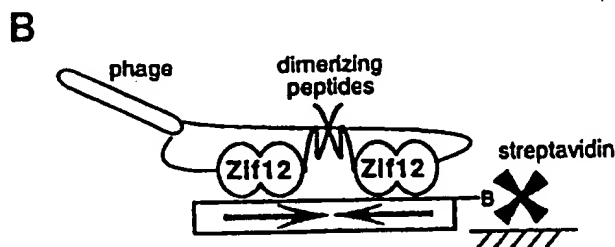
Dimerizing peptide

Here, the original claims recited fusion proteins comprising "zinc finger proteins" and a "peptide linker" wherein the zinc finger-containing fusion proteins are non-covalently

complexed by “specific binding” of the “nonnaturally occurring” peptide linkers on each zinc finger fusion protein (see, original claim 5, emphasis added)³:

5. A zinc finger complex, comprising a first fusion protein comprising a first zinc finger protein and a first peptide linker and second fusion protein comprising a second zinc finger protein and a second peptide linker, wherein the first and second fusion proteins are complexed by **specific binding** of the first and second peptide linkers and wherein the first and second peptide linkers are **non-naturally** occurring peptides.

Further, the specification as filed includes unambiguous description of various embodiments, including the claimed embodiment in which zinc finger-containing fusion proteins are complexed to each other by specific binding of non-naturally-occurring dimerizing peptides to each other (FIG. 3B and page 3, lines 26-32):



The invention also provides zinc finger complexes. Such a complex comprises a first fusion protein comprising a first zinc finger protein and a first peptide linker and a second fusion protein comprising a second zinc finger protein and a second peptide linker. The first and second fusion proteins are complexed by specific binding of the first and second peptide linkers, and the first and second peptide linkers are nonnaturally occurring peptides. In some complexes, the first and second peptide linkers are first and second copies of the same linker.

³ Appellants also stress that original claim 5 differs from pending claim 5 in ways that in no way affect written description. For example, the pending claim replaces “first” and “second” with “two or more.”

Moreover, although not required, the specification also exemplifies multiple representative species falling within the scope of the claims. *See, e.g.*, pages 32-35, Figure 4A and Table 1 (page 33) disclosing non-naturally occurring dimerizing peptides 1-6, 1* and 5*.

Zinc finger protein

The specification also contains a clear and detailed disclosure of the zinc finger protein component of the claimed complexes, including the structure of component zinc fingers (page 15, line 24 to page 16, line 28), the function of these proteins in binding to a target site (page 14, lines 11 to 27) and how the structure is correlated to function (*i.e.*, the binding of particular helical sequences to particular target sites). *See*, page 14, line 11 to page 17, line 17. In addition, there were numerous references available at the time of filing regarding natural and engineered zinc finger proteins. *See, e.g.*, references cited in the Background section and on pages 14-17.

In this context, it is well settled that satisfaction of the written description requirement does not require description of that which is known. As set forth in the recent case of *Capon v. Eshhar* 76 USPQ2d 1078 (Fed. Cir. 2005), the Federal Circuit completely rejects the notion that the specification must describe information (*e.g.*, sequence data) that is either known or can readily be determined based on scientific facts (*Capon* at page 15, emphasis added):

The "written description" requirement must be applied in the context of the particular invention and the state of the knowledge. The Board's rule that the nucleotide sequences of the chimeric genes must be fully presented, although the nucleotide sequences of the component DNA are known, is an inappropriate generalization. ...

The "written description" requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution.

In the present case, zinc finger protein sequences can be readily obtained, for example from the various published references and/or by practice of the methods disclosed therein. Moreover, Appellants provide an extensive description of zinc finger proteins, their innate

suitability for being engineered to bind a target sequence of choice, and various engineering methods, including selection and rational design. *See*, for example, the substitute specification at page 7, lines 18-27; and page 14, line 11 through page 17, line 17). Curiously, the Examiner asserts that this inclusive description of the various methods for engineering zinc finger proteins is somehow confusing (Examiner's Answer, pp. 8-9). In fact, the variety of different methods of engineering zinc finger proteins reflect the flexibility and wide applicability of the zinc finger domain as a sequence-specific DNA-binding module. That a number of different engineering methods are disclosed is simply an accurate description of the state of the art and is in no way confusing to one of skill in the art.

Turning to the various cases cited in the Examiner's Answer, Appellants reiterate that the written description inquiry is entirely fact-dependent. As such, the holdings in the various cases cited in the Answer are particular to the facts of those cases. In point of fact, the specification at issue in every case cited by the Examiner did not contain literal description (or exemplification) of the claimed subject matter. Appellants' specification contains precisely such literal support and exemplification and, accordingly, possession of the claimed subject matter has been established.

In conclusion, literal description of both zinc finger proteins and dimerizing peptide linkers is present in the original claims, drawings and description. Moreover, exemplification of multiple embodiments of zinc finger proteins and dimerizing peptides is also provided. Combined with the general knowledge available at the time of filing, it is clear that the skilled artisan would have no doubt that Appellants were in full possession of the claimed subject matter at the time of filing. There is nothing the Examiner has set forth (or ever could set forth) that has overcome the presumption of adequate description coupled with literal support. Accordingly, the rejection cannot stand and should be withdrawn.

4. The Claims are Definite and Precise

The rejection of claim 5 under 35 U.S.C. § 112, second paragraph for reciting "two or more" was not reiterated in the Examiner's Answer. (Examiner's Answer, page 5). Thus, the

remaining rejection under 35 U.S.C. § 112, 2nd paragraph centers on whether the term “non-naturally occurring” is sufficiently definite. (Examiner’s Answer, pages 5 and 11-13).

Appellants remind the Examiner that the definiteness requirement of 35 U.S.C. § 112, second paragraph is satisfied if it is clear to the skilled artisan what is meant by a particular claim term. *See, e.g., In re Marosi*, 218 USPQ 289 (Fed. Cir. 1983). Further, the definiteness and clarity of claim language must be analyzed, not in a vacuum, but in light of (1) the content of the particular disclosure; (2) the teachings of the art; and (3) the claim interpretation that would be given by one possessing ordinary skill in the pertinent art at the time the invention was made. *See, e.g., W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 220 USPQ 202 (Fed. Cir. 1983). In other words, the terms at issue must be read in context of the application and field of endeavor.

Against this background, the Examiner’s assertion that the limitation “non-naturally-occurring” recites what is obvious (Examiner’s Answer, page 12) is not understood. Dimerizing peptides can be naturally-occurring or they can be non-naturally-occurring; the claims recite dimerizing peptides that are non-naturally-occurring.

Any concern that the term “non-naturally-occurring” is indefinite because knowledge of what is naturally-occurring may change with time is unfounded. At any point in time, it is a simple and straightforward matter for one of skill in the art to determine what is or is not naturally-occurring; thereby determining the scope of the claims.

Thus, Appellants assert that claims 5, 6 and 20 reasonably apprise those skilled in the art of the metes and bounds of the claimed subject matter.⁴ Accordingly, the rejection cannot be sustained.

5. Pomerantz Does Not Anticipate Claims 5 and 20

Although the rejections based on Kim *et al.* have been withdrawn, claims 5 and 20 remain rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Pomerantz. (Examiner’s Answer, pages 5-6 and pages 13-14). As previously, Pomerantz is alleged to disclose “a zinc finger complex comprising the same zinc fingers 1 and 2 from ZIF268 with a dimerizing peptide

⁴ particularly in contrast to naturally-occurring dimerizing peptides (*e.g.*, see Section 5 of this Reply Brief)

and linker from GAL4 that forms a dimer with a target. [citing page 966, Materials and Methods and RESULTS starting at page 967].” (Examiner’s Answer, pages 5-6). In response to the argument presented by Appellants in their Appeal Brief, that Pomerantz discloses a naturally occurring dimerizing peptide from GAL4, the Examiner stated that Pomerantz’s Abstract indicates that the dimerizing linker is a “portion” of Gal4 and, consequently, is in some way not naturally occurring. (Examiner’s Answer, pages 13-14). In attempting to support this assertion, the Examiner refers to Appellants’ definition of the term “nonnaturally-occurring,” as follows:

Read in light of the specification definition of a non-naturally occurring peptide linkers e.g., less than 50% (amino acid) with natural sequences the GAL4 (41-100 residues) is less than 50% of the naturally occurring sequence of Gal. (Examiner’s Answer, pages 13-14, emphasis in original)

Thus, the Examiner argues that, because the fragment of the GAL4 protein (amino acids 41-100) used by Pomerantz as a dimerizing linker contains less than 50% of the amino acids of the full-length GAL4 protein, it is somehow a non-naturally occurring peptide sequence.

However, in paraphrasing Appellants’ definition of “non-naturally-occurring,” the Examiner omits the antecedent term “sequence identity.” *See* the substitute specification at page 8, lines 3-8, where the definition is presented:

Conversely, the term nonnaturally-occurring is used to describe objects and sequences not found in nature. Preferred nonnaturally occurring sequences show no significant sequence identity, e.g., less than 50% (amino acid or nucleotide) with natural sequences, in distinction from induced mutations of natural sequences. Typically, nonnaturally occurring sequences do not contain a contiguous segment of at least half their length with a natural protein. (Emphasis added)

Thus, to fall under Appellants’ definition of non-naturally-occurring, a sequence must have less than 50% sequence identity with a natural sequence. A peptide having less than 50% of the length of a natural protein is not a non-naturally-occurring sequence, according to this definition. Thus, when tested by the proper criterion, it is clear that the GAL4 fragment used by

Pomerantz is not a non-naturally-occurring peptide, because it has 100% sequence identity with the portion of GAL 4 from which it was obtained.


It thus appears that this anticipation rejection is based on the Examiner's contortion of Appellants' definition of "non-naturally occurring." As shown above, such an interpretation is contrary to the meaning of the term in the art, and is contrary to Appellants' definition of the term. Because Pomerantz discloses a naturally-occurring dimerizing peptide, he does not describe or demonstrate the elements of the claims on appeal. Accordingly, the rejection should be reversed.

CONCLUSION

For the reasons stated above, Appellants respectfully submit that the pending claims are fully described by the specification as filed, are clear and definite, and are novel and unobvious over the cited reference. Accordingly, Appellants request that the rejection of the claims on appeal be reversed, and that the application be remanded to the Examiner so that the appealed claims can proceed to allowance.

Respectfully submitted,

Date: November 9, 2005

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CLAIMS APPENDIX



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CLAIMS INVOLVED IN THE APPEAL

1 to 4. (canceled).

5. (previously presented): A zinc finger complex, comprising two or more fusion proteins, each fusion protein comprising a zinc finger protein and a peptide linker, wherein the fusion proteins are joined to each other by specific binding of the peptide linkers, and wherein the peptide linkers are non-naturally occurring peptides.

6. (previously presented): The zinc finger complex of claim 5, wherein the peptide linker of each fusion protein has the same sequence.

7-19. (canceled).

20. (previously presented): The zinc finger complex of claim 5, wherein the zinc finger protein of each fusion protein has the same sequence.